

REMARKS

Claims 10-19 are currently pending in the application. Claims 10-19 are rejected. As noted, through this response, claims 10 to 13 and 15 to 19 have been amended to recite more distinctly the invention of this application, and to overcome the outstanding rejections as discussed in detail below. Applicants respectfully traverse the outstanding rejections as set forth below.

REJECTIONSSection 2 of the Office Action - Rejection under 35 USC 112 second paragraph

The examiner maintains that applicants did not obviate the ambiguity cited by the examiner as the basis for the previous rejection by the arguments put forth. The examiner asks "What is the claimed product? Is it anhydrous solvate or is it solvate/hydrate. Please note that the same process of the instant specification and the issued patent cannot make two different product[s]. Applicants must clearly define in the claim what is the chemical nature of the product."

Applicant has considered the rejection under 35 USC 112 second paragraph and the questions posed by the Examiner. To clearly define the chemical nature of the product, claims 10-13 and 15-19 were amended to insert the word "anhydrous" immediately before the phrase "Form II of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride ethanol solvate" and elsewhere in the amended claims as would be appropriate. Claim 14 is dependent on claim 13 and was previously presented.

It is respectfully submitted that, by these amendments, claims 10-19 particularly point out and distinctly claim the subject matter which applicant regards as his invention. In view of the foregoing it is respectfully requested that the outstanding rejection to claims 10 to 19 be withdrawn.

Section 3 of the Office Action - Rejection under 35 U.S.C. § 102(f)

Claims 10-19 stand rejected again under 35 USC 102(f) for the reason of record. The examiner maintains "that the two declarations [one from inventor Kesseler of the instant application and the second from the inventors of US 6,576,647 (hereinafter '647 Patent)] stated that the Example 4 procedure [of the '647 Patent] was invented by Kesseler." The examiner alleges that "it is unclear 'what' is the product being made by Example 4 procedure, is it a solvate/hydrate or is it an anhydrous solvate. Therefore, the two declarations did not obviate the 102(f) issue between the solvate/hydrate of the '647 patent and the instant claim."

After reviewing a proposed draft response to the instant office action, the examiner specifically indicated that the issue at hand results from "Form II" in the '647 Patent being described in column 3, lines 47-51, as "the solvate/hydrate of ethanol/water of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride as described by x-ray powder diffraction in Table 2, obtained using Cu-K-alpha radiation.", and alleges that it "is unclear 'what' is the product being made by example 4 procedure, is it a solvate/hydrate or is it an anhydrous solvate." Furthermore, the examiner alleges that "the same process of the instant specification and the issued patent cannot make two different products." The examiner suggested that a declaration from the inventors of the '647 Patent be filed stating the correct nature of the Form II material and linking the product of Example 4 with the X-ray powder diffraction data of Table II in the aforesaid '647 Patent. The examiner further suggested that a certificate of correction be filed to correct the description of Form II in the specification of the '647 Patent if said Form II material had been inadvertently described as a solvate/hydrate versus an anhydrous solvate.

As part of this response, a declaration by the inventors of the '647 Patent is attached which states, in paragraph 2, that the procedure of Kesseler, disclosed as example 4 of the '647 Patent, was used to prepare anhydrous Form II of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride ethanol solvate that is characterized by the X-ray powder diffraction data presented in Table 2 of the '647 Patent. In addition, three sentences in the '647 Patent were noted to require correction due to the inadvertent description of the Form II material as a

"solvate/hydrate" as presented in paragraphs 5 to 7 of the declaration. The sentence appearing in column 3, lines 47-51, of the '647 Patent, specifically noted by the Examiner in her comments on the first draft response, is presented in paragraph 6 of the declaration and should properly read "Form II" means the ethanol solvate of anhydrous (-)cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride as described by X-ray powder diffraction in Table 2, obtained using Cu K-alpha radiation." In addition, the inventors of the '647 Patent noted that the sentence in column 1, lines 36-38, reads "The preferred form is the Flavopiridol hydrochloride ethanol/water solvate form (hereafter "Form II")." and should read --The preferred form is the Flavopiridol hydrochloride ethanol solvate form (hereafter "Form II").--(paragraph 5), and that the sentence in column 4, lines 64-65, reads "Form II, as a solvate/hydrate, showed a slow but continual weight gain of about 4% through about 60% Relative Humidity." and should read --Form II showed a slow but continual weight gain of about 4% through about 60% Relative Humidity.--(paragraph 7). A request for the issuance of a certificate of correction for US 6,576,647 B2 was filed and a copy of the request for a certificate of correction as filed accompanies this response.

Applicant submits that the 35 U.S.C. § 102(f) rejection is now resolved by:

1. the previously submitted two declarations that clarified Kesseler is the true inventor of the Example 1 process of the instant application and the unclaimed Example 4 process of the '647 Patent,
2. the declaration accompanying this response by the inventors of the '647 Patent acknowledging inadvertent errors in the '647 patent specification pertaining to the description of the Form II material as a "solvate/hydrate of ethanol/water" and acknowledging that the Form II material as prepared by the Example 4 procedure obtained from Kesseler is the anhydrous (-)cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride ethanol solvate as characterized by X-ray powder diffraction in Table 2, and
3. a copy of the request for a certificate of correction for the '647 Patent most notably correcting the description of the Form II material prepared by the method of Kesseler as being the ethanol solvate of anhydrous (-)cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride as described by X-ray powder diffraction in Table 2, obtained using Cu K-

alpha radiation in addition to correction of two other sentences wherein the Form II material is inadvertently characterized as an "ethanol/water solvate" or a "solvate/hydrate".

It is now clear that the identical product is obtained from both Example 1 of the instant application and Example 4 of the '647 Patent, and that product is anhydrous Form II of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride ethanol solvate.

Section 4 of the Office Action - Rejection under 35 USC 112 first paragraph

Claims 10-19 were rejected again under 35 USC 112 first paragraph for reason of record. The examiner notes "applicants argued that Form II was hygroscopic and it is difficult to dry and the issued patent employed the identical procedure to make Form II which contains water. Applicants argument that the instant application did not name its Form II to have other elements such as water is not supportive of the enabling issue[d] as evidence by the record. Since applicants argued that Form II is hy[d]groscopic, and '647 used the same procedure as the instant application, just because applicants did not name water doe not provide description or enablement that how was the water driven out especially applicants argued that the product is hyg[d]roscopic and hard to dry. Such argument is self conflicting."

Applicant again respectfully traverses this rejection. Applicant has never stated, as suggested above by the Examiner, that procedure of Example 1 in the instant application, that is identical to the Example 4 procedure of the '647 Patent, "makes Form II which contains water." On the contrary, Applicant maintains now, as was maintained in previous responses, that the Example 1 procedure provides anhydrous Form II of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride ethanol solvate. The Example 1 process removes any water that may have been present and one skilled in the art recognizes that this process would remove water to provide an anhydrous product. The accompanying declaration and the request for a certificate of correction filed by the inventors of the '647 Patent resolves the issue of the nature of the Form II material prepared by Example 4 of the '647 Patent as discussed above.

Furthermore, a study is described in '647 Patent (column 6, lines 24-40) wherein the Form II material of Example 4 is exposed to various relative humidities. It is clear to one skilled in the art that the '647 Patent clearly states that Form II showed slow but continual weight gain through about 60% relative humidity of approximately 4% [this corresponds to approximately one mole of water per mole of the hydrochloride ethanol solvate], and that variable humidity X-ray powder diffraction showed, that as the humidity is increased there is an apparent decrease in the crystallinity in Form II and a significant change in the X-ray powder diffraction pattern which is presumably due to the loss of ethanol. It is clear from this portion of the specification that the inventors were aware of the fact that Form II is anhydrous and that the absorption of water leads to significant changes in the X-ray powder diffraction pattern of the anhydrous Form II material.

Thus it is clear from the above arguments that the instant specification properly enables the claims, that the claimed product is anhydrous Form II of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8-[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one hydrochloride ethanol solvate and that the presence of moisture would lead to significant changes in the characteristic X-ray diffraction patterns as recited in the specification and claims for the anhydrous Form II material. Applicant respectfully maintains that the specification contains a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same.

In view of the foregoing, Applicants respectfully request reconsideration, withdrawal of all rejections and prompt Notice of Allowance.

CONCLUSION

For all the reasons advanced above, Applicant respectfully submits that claims 10-19 are in condition for immediate allowance and respectfully requests a notice to this effect. Should the Examiner have any questions please call (collect if necessary) the undersigned agent at the telephone number listed below.

The Commissioner is hereby authorized to charge these fees and any other fees that are due to this paper to Deposit Account No. **18-1982** for Aventis Pharmaceuticals Inc., Bridgewater, NJ. Please credit any overpayment to Deposit Account No. **18-1982**.

Respectfully submitted,

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